

***Remarks***

The Applicants thank Examiners David Steadman and Rebecca Prouty for their courtesy and helpful suggestions extended during a telephone interview on October 15, 2002. The Applicants also thank Examiner Steadman for his clarification in a separate telephone discussion on October 16, 2002, that the inclusion of claim 107 in the rejection on page 2, paragraph 4, under 35 U.S.C. § 112, for lack of written description was a typographical error and the claim was in fact, allowable as indicated on pages 1 and 2 of the Advisory Action.

The Applicants respectfully request entry of the proposed amendment by the Examiner. The amendments are believed to place the claims in condition for allowance. Additionally, the claims do not raise new issues that would require further consideration and/or search, they do not raise the issue of new matter, and there are no additional claims presented. The amendments to claims 21, 43, 65, 79 and 80 are merely rewording of the claim language and introduce no new matter. New claims 114 and 115 are independent claims that lists individual embodiments of claims 21 and 65 and thus, no new matter or new issues are introduced.

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 21, 25, 33-35, 38-43, 47, 55-57, 60-65, 67, 68, 72-85 and 103-115 are pending in the application, with claims 21, 43, 65, 79, 80, 107, 114 and 115 being the independent claims. The Examiner stated in Paper No. 21 that claims 103-112 were in condition for allowance; claims 25, 47, 67, 68 and 72-75 were objected to for being dependent upon a rejected claim; and claims 21-24, 26-46, 48-66, 69-71 and 76-102 were rejected.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112***

The Applicants acknowledge, with appreciation, the withdrawal of the rejections of claims 37, 59, 80, 94 and 107 under 35 U.S.C. § 112, second paragraph.

The Examiner maintained the rejection of claims 21-24, 26-46, 48-66, 69-71, 76-102 and 107 in Paper 21. The Examiner stated that the claims are not so limited to polynucleotides encoding polypeptides exhibiting the "structural characteristics" as disclosed at page 13, lines 13-26 of the specification. The Examiner also acknowledges sufficient written description of claim 21, parts (e) and (f) and claim 65 parts (b), (c), and (g)-(j).

While the Applicants do not acquiesce to the position of the Examiner, the cancellation of claims 37, 59, 86, and 94 without prejudice, and the amendment to claims 21, 43, 65, 79, and 80 is believed to overcome the rejection. As discussed *supra*, the maintenance of the rejection of claim 107 was a typographical error, and the claim is allowable. The Applicants thus respectfully request that the rejection be withdrawn.

The Applicants gratefully acknowledge the withdrawal of the rejection of claim 107 under 35 U.S.C. § 112, first paragraph.

The Examiner maintained the rejection of claims 21-24, 26-46, 48-66, 69-71, and 76-102 under 35 U.S.C. § 112, first paragraph. The Examiner maintains that there is no guidance in the specification that the fragments listed in parts (a)-(d) and (g)-(m) of claim 21 or in parts (a) and (d)-(f) of claim 65 have C5 epimerase activity and thus it would be "highly unpredictable that if such fragments were found within a larger polypeptide that the larger polypeptide would exhibit C5-epimerase activity."

While the Applicants do not acquiesce to the position of the Examiner, the amendment of claims 21, 43, 65, 79, and 80 and cancellation of claims 26-32, 36, 37, 48-46, 58, 59, 66, 69-71, and 86-102 should obviate this rejection. The Applicants thus respectfully request that the rejection be withdrawn.

### *Conclusion*

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Advisory Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Amendment and Reply  
is respectfully requested.

Respectfully submitted,

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**Version with markings to show changes made**

Pending claims 21, 43, 65, 79 and 80 were substituted with the following claims 21, 43, 65, 79 and 80:

21.(Twice amended) An isolated polynucleotide comprising a nucleotide sequence encoding a glucuronyl C5-epimerase capable of converting D-glucuronic acid to L-iduronic acid, the amino acid sequence of which is at least 95% identical to a reference amino acid sequence selected from the group consisting of:

- (a) [amino acids 1 to 45 of SEQ ID NO: 13;
- (b) amino acids 25 to 45 of SEQ ID NO: 13;
- (c) amino acids 74 to 86 of SEQ ID NO: 13;
- (d) amino acids 77 to 97 of SEQ ID NO: 13;
- (e)] amino acids 25 to 444 of SEQ ID NO: 13[;] and
- [(f)](b) amino acids 1 to 444 of SEQ ID NO: 13[;
- (g) SEQ ID NO: 2;
- (h) SEQ ID NO: 3;
- (i) SEQ ID NO: 4;
- (j) SEQ ID NO: 5;
- (k) SEQ ID NO: 6;
- (l) SEQ ID NO: 7 and
- (m) SEQ ID NO: 8].

43.(Thrice amended) An isolated polynucleotide encoding a glucuronyl C5-epimerase capable of converting D-glucuronic acid to L-iduronic acid and which hybridizes under the conditions of incubation at 65° C in a solution comprising: 6x SSC, 5x Denhardt's solution containing 0.1% SDS and 0.1 mg/ml denatured salmon sperm DNA, followed by washing in 2x SSC and 0.5% SDS at 42° C, to a polynucleotide encoding a polypeptide selected from the group consisting of:

- (a) [amino acids 1 to 45 of SEQ ID NO: 13;
- (b) amino acids 25 to 45 of SEQ ID NO: 13;
- (c) amino acids 74 to 86 of SEQ ID NO: 13;
- (d) amino acids 77 to 97 of SEQ ID NO: 13;
- (e)] amino acids 25 to 444 of SEQ ID NO: 13[;] and
- [(f)](b) amino acids 1 to 444 of SEQ ID NO: 13[;
- (g) SEQ ID NO: 2;
- (h) SEQ ID NO: 3;
- (i) SEQ ID NO: 4;
- (j) SEQ ID NO: 5;
- (k) SEQ ID NO: 6;
- (l) SEQ ID NO: 7 and
- (m) SEQ ID NO: 8].

65.(Thrice amended) An isolated polynucleotide, or an isolated complementary polynucleotide, which encodes a polypeptide having glucuronyl C5-epimerase activity and capable of converting D-glucuronic acid to L-iduronic acid, and which hybridizes under the conditions of incubation at 65° C in a solution comprising: 6x SSC, 5x Denhardt's solution containing 0.1% SDS and 0.1 mg/ml denatured salmon sperm DNA, followed by washing in 2x SSC and 0.5% SDS at 42° C, to said isolated polynucleotide selected from the group consisting of:

- (a) [nucleotides 73 to 207 of SEQ ID NO: 12;
- (b)] nucleotides 73 to 1404 of SEQ ID NO: 12;
- [(c)](b) nucleotides 73 to 3085 of SEQ ID NO: 12;
- [(d) nucleotides 145 to 207 of SEQ ID NO: 12;
- (e) nucleotides 292 to 329 of SEQ ID NO: 12;
- (f) nucleotides 301 to 362 of SEQ ID NO: 12;
- (g)](c) nucleotides 145 to 1404 of SEQ ID NO: 12;
- [(h)](d) nucleotides 145 to 3085 of SEQ ID NO: 12;
- [(i)](e) nucleotides 1 to 1404 of SEQ ID NO: 12 and
- [(j)](f) nucleotides 1 to 3085 of SEQ ID NO: 12.

79.(Twice amended) The polynucleotide of claim 65, wherein said polynucleotide sequence is selected from a member of the group consisting of

- (a) [nucleotides 73 to 207 of SEQ ID NO: 12;
- (b)] nucleotides 73 to 1404 of SEQ ID NO: 12;
- [(c)](b) nucleotides 73 to 3085 of SEQ ID NO: 12;
- [(d) nucleotides 145 to 207 of SEQ ID NO: 12;
- (e) nucleotides 292 to 329 of SEQ ID NO: 12;
- (f) nucleotides 301 to 362 of SEQ ID NO: 12;
- (g)](c) nucleotides 145 to 1404 of SEQ ID NO: 12;
- [(h)](d) nucleotides 145 to 3085 of SEQ ID NO: 12;
- [(i)](e) nucleotides 1 to 1404 of SEQ ID NO: 12 and
- [(j)](f) nucleotides 1 to 3085 of SEQ ID NO: 12;

and wherein said polynucleotide encodes a fusion protein.

80.(Thrice amended) A polynucleotide which encodes an amino acid sequence which has a deletion of the N-terminal, C-terminal or internal regions of the amino acid sequence encoded by the polynucleotide of claim 65, and wherein said polynucleotide sequence is selected from a member of the group consisting of

- (a) [nucleotides 73 to 207 of SEQ ID NO: 12;
- (b)] nucleotides 73 to 1404 of SEQ ID NO: 12;
- [(c)](b) nucleotides 73 to 3085 of SEQ ID NO: 12;
- [(d) nucleotides 145 to 207 of SEQ ID NO: 12;
- (e) nucleotides 292 to 329 of SEQ ID NO: 12;
- (f) nucleotides 301 to 362 of SEQ ID NO: 12;
- (g)](c) nucleotides 145 to 1404 of SEQ ID NO: 12;
- [(h)](d) nucleotides 145 to 3085 of SEQ ID NO: 12;
- [(i)](e) nucleotides 1 to 1404 of SEQ ID NO: 12 and
- [(j)](f) nucleotides 1 to 3085 of SEQ ID NO: 12.

Claims 114 and 115 were added.

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